

We Claim:

1. An isolated Pro104 antibody that binds to Pro104 on a mammalian cell in vivo.
- 5 2. The antibody of claim 1 which internalizes upon binding to Pro104 on a mammalian cell in vivo.
3. The antibody of claim 1 or claim 2 which is a monoclonal antibody.
- 10 4. The antibody of claim 1 or claim 2 which is an antibody fragment.
5. The antibody of claim 1 or claim 2 which is a chimeric or a humanized antibody.
- 15 6. The antibody of claim 3 which is produced by a hybridoma selected from the group consisting of American Type Culture Collection accession number PTA-5277, 6076, 6077 and 6078.
7. The antibody of claim 3, wherein the antibody competes for binding to the same epitope as the epitope bound by the monoclonal antibody produced by a hybridoma selected from the group consisting of ATCC accession number PTA-5277, 6076, 6077 and 6078.
- 20 8. The antibody of claim 3 which is conjugated to a growth inhibitory agent.
- 25 9. The antibody of claim 3 which is conjugated to a cytotoxic agent.
10. The antibody of claim 9 wherein the cytotoxic agent is selected from the group consisting of toxins, antibiotics, radioactive isotopes and nucleolytic enzymes.
- 30 11. The antibody of claim 10 wherein the cytotoxic agent is a toxin.

12. The antibody of claim 11, wherein the toxin is selected from the group consisting of ricin, saponin, maytansinoid and calicheamicin.

13. The antibody of claim 12, wherein the toxin is a maytansinoid.

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14. The antibody of claim 3, wherein the mammalian cell is a cancer cell.

15. An anti-Pro104 monoclonal antibody that selectively binds a Pro104-expressing cell.

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16. An anti-Pro104 monoclonal antibody that inhibits the growth of Pro104-expressing cancer cells in vivo.

17. The antibody of claim 16 which is a humanized or human antibody.

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18. The antibody of claim 17 which is produced in bacteria.

19. The antibody of claim 15, which is a humanized form of an anti-Pro104 antibody produced by a hybridoma selected from the group consisting of ATCC accession number

20 PTA-5277, 6076, 6077 and 6078.

20. The antibody of claim 16, wherein the cancer cells are from a cancer selected from the group consisting of breast, ovarian, pancreatic and lung cancer.

25 21. The antibody of claim 20, wherein the cancer cell are ovarian or pancreatic cancer cells.

22. A cell that produces the antibody of claim 3.

30 23. The cell of claim 22, wherein the cell is selected from the group consisting of hybridoma cells deposited under American Type Culture Collection accession number PTA-5277, 6076, 6077 and 6078.

24. A method of producing the antibody of claim 3 comprising culturing an appropriate cell and recovering the antibody from the cell culture.

5 25. A composition comprising the antibody of claim 3 or claim 15, and a carrier.

26. The composition of claim 25, wherein the antibody is conjugated to a cytotoxic agent.

10 27. The composition of claim 26, wherein the cytotoxic agent is a maytansinoid.

28. The composition of claim 25, wherein the antibody is a human or humanized antibody and the carrier is a pharmaceutical carrier.

15 29. The composition of claim 28, wherein the humanized antibody is a humanized form of an anti-Pro104 antibody produced by a hybridoma selected from the group consisting of ATCC accession number PTA-5277, 6076, 6077 and 6078.

20 30. A method of killing a Pro104-expressing cancer cell, comprising contacting the cancer cell with the antibody of claim 1 or claim 2, thereby killing the cancer cell.

31. The method of claim 30, wherein the cancer cell is selected from the group consisting of breast, ovarian, pancreatic and lung cancer cell.

25 32. The method of claim 31, wherein the cancer cell is an ovarian or pancreatic cancer cell.

33. The method of claim 31, wherein the ovarian cancer is ovarian serous adenocarcinoma or the breast cancer is breast infiltrating ductal carcinoma.

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34. The method of claim 31, wherein the cancer cell is from metastatic breast, ovarian, pancreatic or lung cancer.

35. The method of claim 30, wherein the antibody is an antibody fragment.
36. The method of claim 30 wherein the antibody is a humanized antibody.
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37. The method of claim 30, wherein the antibody is conjugated to a cytotoxic agent.
38. The method of claim 37, wherein the cytotoxic agent is a toxin selected from the group consisting of maytansinoid, ricin, saporin and calicheamicin.

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39. The method of claim 30, wherein the antibody is a humanized form of the antibody produced by a hybridoma selected from the group consisting of ATCC accession number PTA-5277, 6076, 6077 and 6078.
- 15 40. The method of claim 37, wherein the cytotoxic agent is a radioactive isotope.
41. A method of alleviating a Pro104-expressing cancer in a mammal, comprising administering a therapeutically effective amount of the antibody of claim 15 to the mammal.
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42. The method of claim 42, wherein the cancer is selected from the group consisting of breast, ovarian, pancreatic and lung cancer.
43. The method of claim 42 wherein the ovarian cancer is ovarian serous
25 adenocarcinoma or the breast cancer is breast infiltrating ductal carcinoma.
44. The method of claim 41, wherein the antibody is a humanized antibody.
45. The method of claim 41, wherein the antibody is conjugated to a cytotoxic agent.
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46. The method of claim 40, wherein the cytotoxic agent is a maytansinoid.

47. The method of claim 46, wherein the antibody is administered in conjunction with at least one chemotherapeutic agent.

48. The method of claim 47 wherein the chemotherapeutic agent is paclitaxel or
5 derivatives thereof.

49. An article of manufacture comprising a container and a composition contained therein, wherein the composition comprises an antibody of claim 3.

10 50. The article of manufacture of claim 49 further comprising a package insert indicating that the composition can be used to treat breast, ovarian, pancreatic or lung cancer.

51. A method for determining if cells in a sample express Pro104 comprising
15 (a.) contacting a sample of cells with a Pro104 antibody of claim 3 under conditions suitable for specific binding of the Pro104 antibody to Pro104 and
(b.) determining the level of binding of the antibody to cells in the sample, or the level of Pro104 antibody internalization by cells in said sample,
20 wherein Pro104 antibody binding to cells in the sample or internalization of the Pro104 antibody by cells in the sample indicate cells in the sample express Pro104.

25 52. The method of claim 51 wherein said sample of cells are contacted with an antibody produced by a hybridoma selected from the group of consisting of ATCC accession number PTA-5277, 6076, 6077 and 6078.

53. The method of claim 51 wherein said sample of cells is from a subject who has a cancer, is suspected of having a cancer or who may have a predisposition for developing cancer.

30 54. The method of claim 53 wherein the cancer is breast, ovarian, pancreatic or lung cancer.

55. The method of claim 51 wherein said antibody is a labeled antibody.
56. A method for detecting Pro104 overexpression in a test cell sample, comprising:
- 5 (a.) combining a test cell sample with a Pro104 antibody of claim 3 under conditions suitable for specific binding of Pro104 to Pro104 expressed by cells in said test sample
- 10 (b) determining the level of binding of the Pro104 antibody to the cells in the test sample,
- 10 (c) comparing the level of Pro104 antibody bound to the cells in step (b) to the level of Pro104 antibody binding to cells in a control cell sample, wherein an increase in the binding of the Pro104 antibody in the test cell sample as compared to the control is indicative of Pro104 overexpression by cells in the test cell sample.
- 15 57. The method of claim 56 wherein the test cell sample is a cancer cell sample.
58. The method of claim 57 wherein the cancer cell sample is of breast, ovarian, pancreatic or lung cancer.
- 20 59. The method of claim 58 wherein the ovarian cancer is ovarian serous adenocarcinoma or the breast cancer is breast infiltrating ductal carcinoma.
- 25 60. The method of claim 57 wherein the control is a sample of adjacent normal tissue.
61. A method for detecting Pro104 overexpression in a subject in need thereof comprising,
- 30 (a.) combining a serum sample of a subject with a Pro104 antibody of claim 3 under conditions suitable for specific binding of the Pro104 antibody to Pro104 in said serum sample
- 30 (b.) determining the level of Pro104 in the serum sample,

(c.) comparing the level of Pro104 determined in step b to the level of Pro104 in a control,

wherein an increase in the level of Pro104 in the serum sample from the subject as compared to the control is indicative of Pro104 overexpression in the subject.

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62. The method of claim 61 wherein the subject has cancer.

63. The method of claim 62 wherein the subject has breast, ovarian, pancreatic or lung cancer or a metastatic cancer thereof.

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64. The method of claim 63 wherein the ovarian cancer is ovarian serous adenocarcinoma or the breast cancer is breast infiltrating ductal carcinoma..

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65. The method of claim 61 wherein the control is a serum sample from a subject without a cancer overexpressing Pro104.

66. A screening method for antibodies that bind to an epitope which is bound by an antibody of claim 3 comprising,

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(a.) combining a Pro104-containing sample with a test antibody and an antibody of claim 3 to form a mixture ,

(b.) determining the level of Pro104 antibody bound to Pro104 in the mixture and

(c.) comparing the level of Pro104 antibody bound in the mixture of step (a) to a control mixture,

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wherein the level of Pro104 antibody binding to Pro104 in the mixture as compared to the control is indicative of the test antibody's binding to an epitope that is bound by the anti-Pro104 antibody of claim 3.

67. The screening method of claim 66 wherein the level of Pro104 antibody bound to 30 Pro104 is determined by ELISA. .

68. The screening method of claim 66 wherein the control is a mixture of Pro104, Pro104 antibody of claim 3 and an antibody known to bind the epitope bound by the Pro104 antibody of claim 3.
- 5 69. The screening method of claim 66 wherein the anti-Pro104 antibody is labeled.
70. The screening method of claim 69 wherein the Pro104 is bound to a solid support.
71. The screening method of claim 70 wherein the solid support is a sepharose bead.

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